In response to the above rejections, Applicants have amended the claims which, when considered with the following remarks, is deemed to place the present application in condition for allowance or at least in better condition for appeal. Favorable consideration of all pending claims is respectfully requested.

In the first instance, Applicants respectfully submit that the Sequence Listing has been amended to correct certain typographical errors. More specifically, Applicants have corrected two typographical errors in the nucleotide sequence of SEQ ID NO: 6 (human bcl-w) at nucleotide position 301, 404 and 405, as indicated in the attached marked-up copy of the amended Sequence Listing. Furthermore, the protein sequence in SEQ ID NO: 7 has been amended to correct two clerical errors appearing at positions 101 and 135. In addition, Applicants have corrected certain typographical errors in the nucleotide sequence of SEQ ID NO: 8 (murine bcl-w), as indicated in the attached marked-up copy of the amended Sequence Listing. The protein sequence in SEQ ID NO: 9 has been amended to correct certain clerical errors, as indicated in the attached marked-up copy of the amended sequence listing.

Applicants respectfully submit that the foregoing amendment does not introduce new matter. More specifically, the protein sequence of SEQ ID NO: 7 (human bcl-w) as amended is set forth in Figure 8 as originally filed. The protein sequence of SEQ ID NO: 9 (murine bcl-w) as amended is set forth in Figure 1 as originally filed. In addition, these protein sequences find support in Figures 9A and 9B of the priority document, Australian Provisional Application PN8965, filed on March 27, 1996. A courtesy copy of such priority document is enclosed for the Examiner's convenience (Exhibit A). The nucleotide sequences of SEQ ID NO: 6 and SEQ ID NO: 8 as amended are also disclosed in Figure 9A and 9B, respectively, of the priority document.

Applicants further respectfully submit that the originally filed Figures 9A to 9B(iv), which set forth the nucleotide and protein sequences of human bcl-w and murine bcl-w, contain the same typographical errors as the original Sequence Listing. Accordingly, Applicants submit herewith substitute sheets of Figures 9A and 9B to replace the drawing sheets of Figures 9A to 9B(iv) originally filed. The substitute drawing of Figure 9B discloses the nucleotide sequence (SEQ ID NO: 6) and the encoded protein sequence (SEQ ID NO: 7) of human bcl-w. The substitute drawing of Figure 9B discloses the nucleotide sequence (SEQ ID NO: 8) and the encoded protein sequence (SEQ ID NO: 9) of murine bcl-w. These substitute sheets of drawings do not introduce new matter and are fully supported by the application as filed and by the priority document.

Furthermore, Applicants respectfully submit that the foregoing amendment does not introduce matters that require an additional search on the part of the Examiner. In particular, SEQ ID NO: 7 (human bcl-w) is only amended by two amino acid residues of the total 193 amino acid residues. SEQ ID NO: 9 (murine bcl-w) is only amended by 9 out of 193 amino acid molecules. Therefore, the Examiner's initial search for sequences having at least about 47% similarity to the original SEQ ID NO: 7 or original SEQ ID NO: 9, and for nucleotide sequences encoding proteins having at least about 47% similarity to the original SEQ ID NO: 7 or original SEQ ID NO: 9, would have been sufficient to capture the current corrected version of SEQ ID NO: 7 and SEQ ID NO: 9, as well as the corrected versions of the encoding nucleotide sequences SEQ ID NO: 6 and SEQ ID NO: 9.

Turning to the claims, the Examiner rejects claims 1-4 under 35 U.S.C. §112, first paragraph as allegedly not enabled. The Examiner admits that the specification is enabling for an isolated nucleic acid molecule comprising SEQ ID NO: 6 or 8 which encodes the amino acid sequence of SEQ ID NO: 7 or 9. However, the Examiner contends that the specification does

not provide enablement for all nucleic acid molecules encompassed by the claims. The Examiner states that the specification does not disclose any derivative of SEQ ID NO: 6 or 8, or a nucleic acid molecule encoding an amino acid sequence having at least 47% similarity to SEQ ID NO: 7 or 9, or a nucleic acid molecule which hybridizes under low stringency conditions to SEQ ID NO: 6 or 8 and which elicits a Bcl-w-related activity. It is the Examiner's opinion that it would take undue experimentation for those skilled in the art to practice the claimed invention.

Applicants respectfully disagree with the Examiner. Applicants respectfully submit that the present specification adequately teaches the molecules as claimed, including derivative and homologous sequences of SEQ ID NO: 6 or 8 that enhance cell survival. For example, the specification teaches the human bcl-w gene (SEQ ID NO: 6) and the murine bcl-w gene (SEQ ID NO: 8). The specification further teaches that the human Bcl-w protein and the murine Bcl-w share about 90% similarity. Moreover, the specification provides specific exemplification demonstrating that expression of the bcl-w gene enhances cell survival. See pages 35-36 of the specification. In light of the present teaching, those skilled in the art can isolate a nucleic acid molecule that either hybridizes to SEQ ID NO: 6 or 8, or encodes a protein that shares at least about 47% similarity to SEQ ID NO: 7 or 9, and determine whether the isolated molecule enhances cell survival. It is respectfully submitted that the experimentation required for those skilled in the art to make and use the claimed molecule is not undue.

However, in an effort to favorably advance the prosecution of the present case,

Applicants have canceled claims 1-4 without prejudice, rendering the rejection thereof moot.

Applicants reserve the right to pursue the subject matter of these canceled claims in a continuing application.

Applicants have also added claims 21-24, directed to nucleic acid molecules comprising SEQ ID NO: 6 or SEQ ID NO: 8, or encoding a protein having a sequence as set

forth in SEQ ID NO: 7 or SEQ ID NO: 9. As the Examiner has acknowledged in the Final Action, the specification is enabling for these nucleic acid molecules.

Accordingly, withdrawal of the rejection of claims 1-4 under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 1 and 4 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 5,789,201 ("the '201 patent"). According to the Examiner, the '201 patent teaches nucleotide sequences encoding a bcl-2 homolog (bcl-y). The Examiner contends that the sequence search report provided by the Examiner shows that the human bcl-y gene of the '201 patent matches 97.4% to SEQ ID NO: 6 (human bcl-w) of the claimed invention, and 85% to SEQ ID NO: 8 (murine bcl-w) of the present invention; and that the human Bcl-y protein of the '201 patent matches 98.7% to SEQ ID NO: 7 (human Bcl-w).

It is respectfully submitted that the cancellation of claims 1-4 renders the rejection moot. Withdrawal of the rejection is therefore respectfully requested.

Applicants further submit that the nucleic acid molecules of claims 21-24 are not taught by the '201 patent. Applicants have provided herewith **Exhibit B**, illustrating the differences between the bcl-w sequences of the present application and the bcl-y sequences of the '201 patent. At page 1 of Exhibit B, the human bcl-w (SEQ ID NO: 7), the murine bcl-w (SEQ ID NO: 9), the human bcl-y of the '201 patent (SEQ ID NO: 4 of the '201 patent) and the rat bcl-y of the '201 patent are compared with one another. It is observed that the human bcl-w protein of the present application differs from the human bcl-y of the '201 patent at amino acid position 15, with Ala in human bcl-w and Glu in human bcl-y. The human bcl-w protein differs from the rat bcl-y of the '201 patent at amino acid position 7 ("A" in human bcl-w and "T" in rat bcl-y), position 124 ("E" in human bcl-w and "D" in rat bcl-y), and position 128 ("A" in human bcl-w and "T" in rat bcl-y). It is further observed that the murine bcl-w protein of the present

application differs from the human bcl-y of the '201 patent at amino acid position 7 ("T" in murine bcl-w and "A" in human bcl-y), position 15 ("A" in murine bcl-w and "E" in human bcl-y), and position 124 ("D" in murine bcl-w and "E" in human bcl-y). The murine bcl-w protein of the present application also differs from the rat bcl-y of the '201 patent at amino acid position 128 ("A" in murine bcl-w and "T" in rat bcl-y). Accordingly, protein sequences of SEQ ID NO: 7 and SEQ ID NO: 9 of the present application are not taught by the '201 patent, nor are the nucleic acid molecules encoding the protein of SEQ ID NO: 7 or SEQ ID NO: 9 (i.e., the subject matter of claims 21-22) taught by the '201 patent.

At page 2 of Exhibit B, the nucleotide sequence of the human bcl-w gene (SEQ ID NO: 6 of the present application) is compared with the human bcl-y and rat bcl-y genes of the '201 patent. Those nucleotides in the bcl-y genes which differ from the human bcl-w gene are indicated underneath the human bcl-w sequence. Clearly, the human bcl-w gene (SEQ ID NO: 6) of the present application is distinct from the human bcl-y and rat bcl-y genes of the '201 patent. Therefore, claim 23, drawn to a nucleic acid molecule comprising SEQ ID NO: 6, is not taught by the '201 patent.

Page 3 of Exhibit B illustrates the differences between the murine bcl-w gene (SEQ ID NO: 8) of the present application and the bcl-y genes of the '201 patent. Clearly, the murine bcl-w gene (SEQ ID NO: 8) of the present application is distinct from the human bcl-y and rat bcl-y genes of the '201 patent. Therefore, claim 24, drawn to a nucleic acid molecule comprising SEQ ID NO: 8 is not taught by the '201 patent.

Attached hereto is a marked-up copy of the amendment to the claims and to the Sequence Listing, entitled "Version with markings to show changes made"; a substitute paper and computer-readable copy of the Sequence Listing; a statement under §1.821(f) verifying that the content of the substitute paper copy and the substitute computer-readable copy of the

Sequence Listing are the same; substitute sheets for Figures 9A and Figures 9B; Exhibit A and Exhibit B.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

Frank S. DiGiglio Registration No. 31,346

Scully, Scott, Murphy & Presser 400 Garden City Plaza Garden City, New York 11530 Telephone: 516-742-4343 FSD/XZ:ab

Enclosures: Marked up version of the amendment to the claims and the Sequence Listing

Substitute paper and computer-readable copy of the Sequence Listing

Statement under §1.821(f)

Substitute sheets of Figures 9A and 9B

Exhibit A: Priority Document (Australian Provisional Application PN8965)

Exhibit B: Comparison of bcl-w and bcl-y sequences



Serial No:

09/155,327

Date:

August 9, 2001

## **VERSION WITH MARKINGS TO SHOW CHANGES MADE**

## In the claims:

Claims 1-4 have been canceled without prejudice.

Claims 21-24 have been added:

- 21. An isolated nucleic acid molecule, wherein said nucleic acid molecule encodes a protein comprising an amino acid sequence as set forth in SEQ ID NO: 7.
- 22. An isolated nucleic acid molecule, wherein said nucleic acid molecule encodes the amino acid sequence as set forth in SEQ ID NO: 9.
- 23. An isolated nucleic acid molecule wherein said nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 6.
- 24. An isolated nucleic acid molecule wherein said nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 8.

## In the Sequence Listing:

The sequences in SEQ ID NO: 6-9 have been amended as follows:

## AUG 2 1 2001

**TECH CENTER 1600/2900** 

96

/	OIPE
	AU6 1 3 2001
HE	
	& TRADEMPOR

<210> 6 <211> 583 <212> DNA <213> HUMAN

<220>

<221> CDS

<222> (1)..(579)

<400> 6

atg gcg acc cca gcc tcg gcc cca gac aca cgg gct ctg gtg gca gac
Met Ala Thr Pro Ala Ser Ala Pro Asp Thr Arg Ala Leu Val Ala Asp

1 5 10 15

ttt gta ggt tat aag ctg agg cag aag ggt tat gtc tgt gga gct ggc
Phe Val Gly Tyr Lys Leu Arg Gln Lys Gly Tyr Val Cys Gly Ala Gly
20 25 30

ccc ggg gag ggc cca gca gct gac ccg ctg cac caa gcc atg cgg gca 144
Pro Gly Glu Gly Pro Ala Ala Asp Pro Leu His Gln Ala Met Arg Ala
35 40 45

gct gga gat gag ttc gag acc cgc ttc cgg cgc acc ttc tct gat ctg 192
Ala Gly Asp Glu Phe Glu Thr Arg Phe Arg Arg Thr Phe Ser Asp Leu
50 55 60

gcg gct cag ctg cat gtg acc cca ggc tca gcc cag caa cgc ttc acc 240
Ala Ala Gln Leu His Val Thr Pro Gly Ser Ala Gln Gln Arg Phe Thr
65 70 75 80

cag gtc tcc gac gaa ctt ttt caa ggg ggc ccc aac tgg ggc cgc ctt 288 Gln Val Ser Asp Glu Leu Phe Gln Gly Gly Pro Asn Trp Gly Arg Leu 85 90 95

gta gcc ttc ttt  $\frac{g}{g}$ tc ttt ggg gct gca ctg tgt gct gag agt gtc aac 336 Val Ala Phe Phe  $\frac{1}{100}$  Phe Gly Ala Ala Leu Cys Ala Glu Ser Val Asn 100 105 110

aag gag atg gaa cca ctg gtg gga caa gtg cag gag tgg atg gtg gcc 384
Lys Glu Met Glu Pro Leu Val Gly Gln Val Gln Glu Trp Met Val Ala
115 120 125

						ct										
						g <b>t</b>										432
Tyr	Leu	Glu	Thr	Arg	Leu	<del>Val</del>	Asp	Trp	Ile	His	Ser	Ser	Gly	Gly	Trp	
	130					135					140					
gcg	gag	ttc	aca	gct	cta	tac	aaa	gac	aaa	acc	cta	gag	ααα	aca	caa	480
						Tyr										100
145					150	+ 1 +	O ± J	пор	O±3	155	пси	Gra	Gra	лта		
110					100					133					160	
						tgg										528
Arg	Leu	Arg	Glu	Gly	Asn	Trp	Ala	Ser	Val	Arg	Thr	Val	Leu	Thr	Gly	
				165					170					175		
gcc	gtg	gca	ctg	ggg	gcc	ctg	gta	act	gta	ggg	gcc	ttt	ttt	gct	agc	576
Ala	Val	Ala	Leu	Gly	Ala	Leu	Val	Thr	Val	Gly	Ala	Phe	Phe	Ala	Ser	
			180	_				185		-			190			
													100			
220	+ ~ > -	,														F 0 0
-	tgaa	1														583
Lys																
<210	)> 7															
	)> 7 -> 19	3														
<211																
<211 <212	> 19 2> PF	ΥT														
<211 <212	> 19	ΥT														
<211 <212 <213	-> 19 2> PF 3> HU	ΥT														
<211 <212 <213	> 19 2> PF 3> HU	RT JMAN	Document	77.3												
<211 <212 <213 <400 Met	> 19 2> PF 3> HU	RT JMAN	Pro		Ser	Ala	Pro	Asp		Arg	Ala	Leu	Val	Ala	Asp	
<211 <212 <213	> 19 2> PF 3> HU	RT JMAN	Pro	Ala 5	Ser	Ala	Pro	Asp	Thr	Arg	Ala	Leu	Val	Ala 15	Asp	
<211 <212 <213 <400 Met	> 19 2> PF 3> HU	RT JMAN	Pro		Ser	Ala	Pro	Asp		Arg	Ala	Leu	Val		Asp	
<211 <212 <213 <400 Met 1	-> 19 2> PF 3> HU 0> 7 Ala	RT JMAN Thr		5		Ala			10					15	_	
<211 <212 <213 <400 Met 1	-> 19 2> PF 3> HU 0> 7 Ala	RT JMAN Thr		5					10					15	_	
<211 <212 <213 <400 Met 1	-> 19 2> PF 3> HU 0> 7 Ala	RT JMAN Thr	Tyr	5				Lys	10				Gly	15	_	
<211 <212 <213 <400 Met 1	-> 19 2> PF 3> HU 0> 7 Ala Val	RT JMAN Thr Gly	Tyr 20	5 Lys	Leu	Arg	Gln	Lys 25	10 Gly	Tyr	Val	Cys	Gly 30	15 Ala	Gly	
<211 <212 <213 <400 Met 1	-> 19 2> PF 3> HU 0> 7 Ala Val	RT JMAN Thr Gly	Tyr 20	5 Lys	Leu		Gln Asp	Lys 25	10 Gly	Tyr	Val	Cys Ala	Gly 30	15 Ala	Gly	
<211 <212 <213 <400 Met 1	-> 19 2> PF 3> HU 0> 7 Ala Val	RT JMAN Thr Gly	Tyr 20	5 Lys	Leu	Arg	Gln	Lys 25	10 Gly	Tyr	Val	Cys	Gly 30	15 Ala	Gly	
<211 <212 <213 <400 Met 1 Phe	-> 19 2> PF 3> HU 0> 7 Ala Val	Thr Gly Glu 35	Tyr 20 Gly	5 Lys Pro	Leu Ala	Arg Ala	Gln Asp 40	Lys 25 Pro	10 Gly Leu	Tyr His	Val Gln	Cys Ala 45	Gly 30 Met	15 Ala Arg	Gly	
<211 <212 <213 <400 Met 1 Phe	2> 19 2> PF 3> HU 0> 7 Ala Val Gly	Thr Gly Glu 35	Tyr 20 Gly	5 Lys Pro	Leu Ala	Arg	Gln Asp 40	Lys 25 Pro	10 Gly Leu	Tyr His	Val Gln	Cys Ala 45	Gly 30 Met	15 Ala Arg	Gly	
<211 <212 <213 <400 Met 1 Phe	-> 19 2> PF 3> HU 0> 7 Ala Val	Thr Gly Glu 35	Tyr 20 Gly	5 Lys Pro	Leu Ala	Arg Ala	Gln Asp 40	Lys 25 Pro	10 Gly Leu	Tyr His	Val Gln	Cys Ala 45	Gly 30 Met	15 Ala Arg	Gly	
<211 <212 <213 <400 Met 1 Phe	2> 19 2> PF 3> HU 0> 7 Ala Val Gly	Thr Gly Glu 35	Tyr 20 Gly	5 Lys Pro	Leu Ala	Arg Ala Thr	Gln Asp 40	Lys 25 Pro	10 Gly Leu	Tyr His	Val Gln Thr	Cys Ala 45	Gly 30 Met	15 Ala Arg	Gly	
<211 <212 <213 <400 Met 1 Phe Pro	S 19 PF S HU ) 7 Ala Val Gly 50	Thr Gly Glu 35	Tyr 20 Gly Glu	5 Lys Pro	Leu Ala Glu	Arg Ala Thr	Gln Asp 40 Arg	Lys 25 Pro	10 Gly Leu Arg	Tyr His Arg	Val Gln Thr 60	Cys Ala 45 Phe	Gly 30 Met	15 Ala Arg Asp	Gly Ala Leu	
<211 <212 <213 <400 Met 1 Phe Pro	S 19 PF S HU ) 7 Ala Val Gly 50	Thr Gly Glu 35	Tyr 20 Gly Glu	5 Lys Pro	Leu Ala Glu	Arg Ala Thr 55	Gln Asp 40 Arg	Lys 25 Pro	10 Gly Leu Arg	Tyr His Arg	Val Gln Thr 60	Cys Ala 45 Phe	Gly 30 Met	15 Ala Arg Asp	Gly Ala Leu	

Gln Val Ser Asp Glu Leu Phe Gln Gly Gly Pro Asn Trp Gly Arg Leu 85 90 95 Val Val Ala Phe Phe Leu Phe Gly Ala Ala Leu Cys Ala Glu Ser Val Asn 100 105 Lys Glu Met Glu Pro Leu Val Gly Gln Val Gln Glu Trp Met Val Ala 115 120 125 Aca Tyr Leu Glu Thr Arg Leu <del>Val</del> Asp Trp Ile His Ser Ser Gly Gly Trp 130 135 140 Ala Glu Phe Thr Ala Leu Tyr Gly Asp Gly Ala Leu Glu Glu Ala Arg 145 150 155 160

Arg Leu Arg Glu Gly Asn Trp Ala Ser Val Arg Thr Val Leu Thr Gly
165 170 175

Ala Val Ala Leu Gly Ala Leu Val Thr Val Gly Ala Phe Phe Ala Ser 180 185 190

Lys

<210> 8

<211> 58**12** 

<212> DNA

<213> Mouse

<220>

<221> CDS

<222> (1)..(579)

<400> 8

atg  $\frac{g}{2}$ cg acc cca gcc tca acc cca gac aca cg $\frac{g}{2}$  gct cta gtg gct gac 48

Met  $\frac{g}{2}$  Thr Pro Ala Ser Thr Pro Asp Thr Arg Ala Leu Val Ala Asp

1 10 15

+++	αta	aac	tat	agg	ctg	add	cad	aag	aat	tat	atc	tat	gga	act	aa <b>d</b>	96
	_				Leu											
		1	20			,		25	-	-		-	30		-	
cct	ggg	gaa	ggc	cca	gcc	gcc	gac	ccg	ctg	cac	caa	gcc	atg	cgg	gct	144
Pro	Gly	Glu	Gly	Pro	Ala	Ala	Asp	Pro	Leu	His	Gln	Ala	Met	Arg	Ala	
		35					40					45				
_		_			gag											192
Ala	Gly	Asp	Glu	Phe	Glu	Thr	Arg	Phe	Arg	Arg		Phe	Ser	Asp	Leu	
	50					55					60					
														1.4.		240
-	_				gtg											240
	Ala	GIn	Leu	His	Val	Thr	Pro	GLY	Ser	75	GIN	GIN	Arg	rne	80	
65					70					73					00	
cad	att	tcc	aac	gaa	ctt	ttc	caa	aaa	aac	cct.	aac	taa	aac	cat	ctt	288
					Leu											
0111		-		85					90			-	-	95		
gtg	gca	ttc	ttt	gtc	ttt	ggg	gct	gcc	ctg	tgt	gct	gag	agt	gtc	aac	336
Val	Ala	Phe	Phe	Val	Phe	Gly	Ala	Ala	Leu	Cys	Ala	Glu	Ser	Val	Asn	
			100					105					110			
									q				9			
					ttg											384
Lys	Glu	Met	Glu	Pro	Leu	Val		Gln	Val	Gln	Asp		<del>Ile</del> Met	Val	Ala	
		115					120					125				
												- ~+	~~~	~~~	taa	432
					ctg											452
Tyr		GIU	Thr	Arg	Leu	135	ASP	пр	116	птэ	140	261	GIY	GIY	rrp	
	130					133					140					
aca	gag	ttc	aca	act	cta	tac	aaa	gac	aaa	qcc	ctq	gag	ga <b>¢</b>	gca	cgg	480
															Arg	
145	Glu				150	-	_			155			Glu		160	
				۵	1			_			,		,			
cgt	ctg	cgg	gag	gg <b>¢</b>	aac	tgg	gca	t <b>g</b> a	gtg	ag	aca	gtg	øtg	acç	agg	528
Arg	Leu	Arg	Glu	Gly	Asn	Trp	Ala	<del>Val</del> ∽	Ser	Thr Aro	Val	Val	<b>∧</b> Thr	Gly	Ala	→(th next page
				165	1			رمحور	170	9			Leu	175	5	The state of the s

gcc gtg gca ctg ggg gcc ctg gta act gta ggg gcc ttt ttt gct agc Val Ala Leu Gly Ala Leu Val Thr Val Gly Ala Phe Phe Ala Ser 180 185

190

aag tga

page)

5<del>81</del> 582

<210> 9 <211> 19**23** <212> PRT <213> Mouse

Lys

<400> 9 Met Pro Thr Pro Ala Ser Thr Pro Asp Thr Arg Ala Leu Val Ala Asp Phe Val Gly Tyr Arg Leu Arg Gln Lys Gly Tyr Val Cys Gly Ala Gly 20 Pro Gly Glu Gly Pro Ala Ala Asp Pro Leu His Gln Ala Met Arg Ala 40 Ala Gly Asp Glu Phe Glu Thr Arg Phe Arg Arg Thr Phe Ser Asp Leu 50 55 Ala Ala Gln Leu His Val Thr Pro Gly Ser Ala Gln Gln Arg Phe Thr 70 75 Gln Val Ser Asp Glu Leu Phe Gln Gly Gly Pro Asn Trp Gly Arg Leu 85 90 Val Ala Phe Phe Val Phe Gly Ala Ala Leu Cys Ala Glu Ser Val Asn 100 105 Lys Glu Met Glu Pro Leu Val Gly Gln Val Gln Asp Trp 115 120 Tyr Leu Glu Thr Arg Leu Ala Asp Trp Ile His Ser Ser Gly Gly Trp 135 Ala Asp Phe Thr Ala Leu Tyr Gly Asp Gly Ala Leu Glu Asp Ala Arg 145 150 160 Arg Leu Arg Glu Gly Asn Trp Ala Val Ser Th Thr 165 170 Ala Val Ala Leu Gly Ala Leu Val Thr Val Gly Ala Phe Phe Ala Ser  $\sim_{180}$ 

	cca gcc tcg Pro Ala Ser 5			48
	tat aag ctg Tyr Lys Leu 20	 Gly Tyr Va		 96
	ggc cca gca Gly Pro Ala			144
	gag ttc gag Glu Phe Glu		r Phe Ser	192
	ctg cat gtg Leu His Val 70	 _	-	240
	gac gaa ctt Asp Glu Leu 85			288
	ttt gtc ttt Phe Val Phe 100	Leu Cys Al		336
	gaa cca ctg Glu Pro Leu			384
	acg cgg ctg Thr Arg Leu		r Ser Gly	432
	aca gct cta Thr Ala Leu 150	 		 480
	gag ggg aac Glu Gly Asn 165			528
	ctg ggg gcc Leu Gly Ala 180	Val Gly Al		576
aag tgaa Lys				583

atg Met 1	gcg Ala	acc Thr	cca Pro	gcc Ala 5	tca Ser	acc Thr	cca Pro	gac Asp	aca Thr 10	cgg Arg	gct Ala	cta Leu	gtg Val	gct Ala 15	gac Asp	48
ttt Phe	gta Val	ggc Gly	tat Tyr 20	agg Arg	ctg Leu	agg Arg	cag Gln	aag Lys 25	ggt Gly	tat Tyr	gtc Val	tgt Cys	gga Gly 30	gct Ala	ggc Gly	96
cct Pro	GJA āāā	gaa Glu 35	ggc Gly	cca Pro	gcc Ala	gcc Ala	gac Asp 40	ccg Pro	ctg Leu	cac His	caa Gln	gcc Ala 45	atg Met	cgg Arg	gct Ala	144
gct Ala	gga Gly 50	gac Asp	gag Glu	ttt Phe	gag Glu	acc Thr 55	cgt Arg	ttc Phe	cgc Arg	cgc Arg	acc Thr 60	ttc Phe	tct Ser	gac Asp	ctg Leu	192
gcc Ala 65	gct Ala	cag Gln	cta Leu	cac His	gtg Val 70	acc Thr	cca Pro	ggc Gly	tca Ser	gcc Ala 75	cag Gln	caa Gln	cgc Arg	ttc Phe	acc Thr 80	240
cag Gln	gtt Val	tcc Ser	gac Asp	gaa Glu 85	ctt Leu	ttc Phe	caa Gln	ggg Gly	ggc Gly 90	cct Pro	aac Asn	tgg Trp	ggc Gly	cgt Arg 95	ctt Leu	288
		ttc Phe														336
aaa Lys	gaa Glu	atg Met 115	gag Glu	cct Pro	ttg Leu	gtg Val	gga Gly 120	caa Gln	gtg Val	cag Gln	gat Asp	tgg Trp 125	atg Met	gtg Val	gcc Ala	384
tac Tyr	ctg Leu 130	gag Glu	aca Thr	cgt Arg	ctg Leu	gct Ala 135	gac Asp	tgg Trp	atc Ile	cac His	agc Ser 140	agt Ser	ggc Gly	ggc Gly	tgg Trp	432
		ttc Phe													cgg Arg 160	480
cgt Arg	ctg Leu	cgg Arg	gag Glu	ggg Gly 165	aac Asn	tgg Trp	gca Ala	tca Ser	gtg Val 170	agg Arg	aca Thr	gtg Val	ctg Leu	acg Thr 175	Gly	528
gcc Ala	gtg Val	gca Ala	ctg Leu 180	Gly	gcc Ala	ctg Leu	gta Val	act Thr 185	Val	G1A Gaa	gcc Ala	ttt Phe	ttt Phe 190	gct Ala	agc Ser	576
aag Lys	tga															582